This listing of claims will replace all prior versions and listings of claims in the application.

## **Listing of Claims**

- 1. (original) (1) A polypeptide comprising an amino acid sequence consisting of 129th to 3657th amino acids in the amino acid sequence of SEQ ID NO: 2, or (2) a polypeptide exhibiting an SMG-1 activity and comprising an amino acid sequence in which one or plural amino acids are deleted, substituted, and/or inserted at one or plural positions in an amino acid sequence consisting of 129th to 3657th amino acids in the amino acid sequence of SEQ ID NO: 2.
- 2. (original) A polypeptide exhibiting an SMG-1 activity and comprising an amino acid sequence having a 90% or more homology, with an amino acid sequence consisting of 129th to 3657th amino acids in the amino acid sequence of SEQ ID NO: 2, with an amino acid sequence consisting of 1st to 3657th amino acids in the amino acid sequence of SEQ ID NO: 2, or with an amino acid sequence consisting of 107th to 3657th amino acids in the amino acid sequence of SEQ ID NO: 2.
- 3. (original) A polypeptide consisting of the amino acid sequence of SEQ ID NO: 2.
- 4. (currently amended) A polynucleotide encoding the polypeptide according to any one of claims 1 to 3.
- 5. (original) An expression vector comprising the polynucleotide according to claim 4.
- 6. (original) A cell transfected with the expression vector according to claim 5.
- 7. (currently amended) An antibody or a fragment thereof, which binds to the polypeptide according to any one of claims 1 to 3.
- 8. (currently amended) A knock-out non-human animal wherein an expression of a gene encoding the polypeptide according to any one of claims 1 to 3 is partially or completely suppressed.
- 9. (original) A method for screening a substance which modifies an SMG-1 activity of the polypeptide according to any one of claims 1 to 3, comprising the steps of: bringing into contact (1) the polypeptide, (2) Upf1/SMG-2, a fragment thereof capable of being phosphorylated, or a fusion polypeptide comprising Upf1/SMG-2 or the fragment thereof, and (3) a substance to be tested; and

carrying out phosphorylation under the conditions that the polypeptide is brought into contact with Upf1/SMG-2, the fragment thereof, or the fusion polypeptide, and analyzing whether or not Upf1/SMG-2, the fragment thereof, or the fusion polypeptide is phosphorylated.

- 10. (currently amended) A method for screening a substance which modifies an SMG-1 activity of the polypeptide according to any one of claims 1 to-3, comprising the steps of: bringing (1) the polypeptide into contact with (2) a substance to be tested; and carrying out phosphorylation under the conditions that the polypeptide is brought into contact with the substance to be tested, and analyzing whether or not the polypeptide is autophosphorylated.
- 11. (currently amended) An agent for suppressing nonsense-mediated mRNA decay, comprising, as an active ingredient, a substance which is obtained by the screening method according to claim 9 or 10 and modifies an SMG-1 activity of the polypeptide according to any one of claims 1 to 3.
- 12. (original) An agent for suppressing nonsense-mediated mRNA decay, comprising as an active ingredient, an inhibitor of a phosphatidyl inositol kinase related kinase.
- 13. (currently amended) An agent for treating and/or preventing a disease caused by a premature translation termination codon generated by a nonsense mutation, comprising, as an active ingredient, a substance which is obtained by the screening method according to claim 9-or 10 and modifies an SMG-1 activity of the polypeptide according to any one of claims 1 to 3.
- 14. (original) An agent for treating and/or preventing a disease caused by a premature translation termination codon generated by a nonsense mutation, comprising as an active ingredient, an inhibitor of a phosphatidyl inositol kinase related kinase.
- 15. (original) An agent for suppressing nonsense, comprising as an active ingredient, (1) an SMG-1-acitivity-deficient mutant, or an inhibitor of a phosphatidyl inositol kinase related kinase, and (2) an aminoglycoside antibiotic.
- 16. (original) An agent for suppressing nonsense, comprising, as an active ingredient, an SMG-1-acitivity-deficient mutant, or an inhibitor of a phosphatidyl inositol kinase related kinase.
- 17. (original) An agent for promoting nonsense-mediated mRNA decay, comprising as an active ingredient, (1) the polypeptide according to any one of claims 1 to 3, (2) a substance which promotes an SMG-1 activity of the polypeptide, or (3) the polypucleotide according to claim 4.

18. (original) A method for identifying a nonsense mutation point in a gene, comprising the steps of:

culturing a cell to be tested which is obtained from a subject to be tested and may contain a gene having a nonsense mutation by a premature translation termination codon, in the presence of an inhibitor of an SMG-1 activity; and analyzing molecular weight of a polypeptide derived from the gene in the cultured cell.

19. (original) A method for detecting a gene having a nonsense mutation, comprising the

steps of:
culturing at least two groups of cells to be tested which are obtained from a subject to be tested
and may contain a gene having a nonsense mutation by a premature translation termination
codon, in the presence of an inhibitor of an SMG-1 activity and in the absence thereof,
respectively; and

detecting a presence or absence of the difference of an amount of mRNA derived from the gene in the cultured cells.